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(54) Title: INTELLIGENT INHALER PROVIDING FEEDBACK TO BOTH PATIENT AND MEDICAL PROFESSIONAL

(57) Abstract

An inhaler device for aerosol delivery of medication employs a microprocessor and electronic sensors for measuring parameters indicative of a patient's inhalation of airborne medication. The sensors produce output signals representative of parameters which determine the proper delivery of medication to receptor sites in the patient's lungs, such as, the rate of flow of air through the inhaler device to the patient's lungs, the duration of inspiration of the medication, and the volume of medication inhaled. The microprocessor is responsive to the output signals of the sensors and stores a record of inhalation events which can be retrieved remotely or by connecting the microprocessor to a display terminal. The microprocessor makes possible a display of data indicative of the delivery of medication for each inhalation event over a course of treatment, thus providing compliance feedback to both the patient and the medical professional. The microprocessor is programmable for dispensing medication in a predetermined amount and at selected times. The microprocessor also performs logical operations and interpretative calculations on the inspiration data to evaluate the effectiveness of the medication and the patient's compliance with a course of treatment. The microprocessor is programmable for varying dosages and times for dispensing the medication as a function of the measured parameters in order to maximize delivery of medication to the patient.

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INTELLIGENT INHALER PROVIDING FEEDBACK TO BOTH PATIENT AND MEDICAL PROFESSIONAL

10   ## BACKGROUND OF THE INVENTION

Field of Invention

The field of the present invention relates
generally to an inhaler device for aerosol delivery
of medicine. More particularly, the present inven-
15   tion is directed to a device for improving medica-
tion compliance by providing feedback regarding
correct and consistent usage of medicine inhalers to
a patient and/or professional such as a physician,
pharmacist, or therapist. The present invention is
20   further directed to a method by which such
professionals can track the usage of medicine
inhalers between visits, and modify medicinal
therapy based on downloading of this information to
a clinical workstation allowing display and
25   analysis.

The Prior Art

Getting patients to correctly use medicine
inhalers is a major problem. Estimates indicate as
few as one quarter of patients using inhalers do so
30   correctly [Orehek, J., "Patient Error in Use of
Bronchodilator Metered Aerosols," British Medical
Journal, 1:76 (1976); Paterson, I.C. and
G.K. Crompton, "Use of Pressurized Aerosols by
Asthmatic Patients," British Medical Journal, 1:7677
35   (1976); Saunders, K.B., "Misuse of Inhaled Broncho-
dilator Agents," British Medical Journal,

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1:1037-1038 (1965); Shim, C., and M.H. Williams,
"The Adequacy of Inhalation of Aerosol from Canister
Nebulizers;" The American Journal of Medicine,
69:891-894 (1980)]. In addition to unnecessary
patient morbidity and mortality, an unfortunate
consequence is that patients may stop taking their
medications because they are not seeing any or
enough benefit. Conversely, having failed to obtain
expected benefits through prescribed usage, some
patients will overuse medications and thereby
increase the risk of side effects caused by higher
than normal dosages (e.g., fungal infections in the
mouth and throat or nervous system effects caused by
medication absorbed in the gastrointestinal tract).

These problems are especially evident in the
case of aerosol pharmaceuticals delivered by hand-
held inhalers. Hand-held metered dose inhalers
(MDIs) are a preferred method of treatment for
common respiratory ailments, since the delivery of
medication directly to its intended site of action
in the lungs allows a reduction in dosage by an
order of magnitude or greater. However, certain of
these compounds, such as anti-inflammatory cortico-
steroids, may take many weeks of administration
before having a significant effect. Moreover, the
inhalation and breath-holding maneuver required for
successful delivery of aerosol to the lower airways
is counterintuitive and poorly understood by most
patients. Thus, a patient may be compliant in using
the medication when prescribed, but unsuccessful in
using it in the correct manner.

When therapeutic results are not obtained, it
may not be evident to the physician which step(s) in

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the process are the problem. Relevant questions,
for example, are "was the medication not taken at
all?", "was it taken at the correct intervals and in
proper relationship to exposure to allergens or
5   other irritants?", and "was the inhalation performed
correctly?".

Another problem the physician faces is how to
interpret variability in therapeutic response. Is
the variability due to some fundamental change in
10   the patient's condition (e.g., the patient now has a
low-grade upper respiratory infection) or is it
caused by differences in delivered medication
dosage?

Deposition of aerosol medication in the human
15   lung is primarily determined by two processes,
inertial impaction and gravitational sedimentation.
Impaction of aerosols in the lungs occurs primarily
at airway bifurcations, and has been shown in
scintigraphic studies to increase as a function of
20   flow rate. Sedimentation involves gravitational
settling of aerosol particles on the airways and
alveoli. Newman, S.P., Pavia, D., Garland, N. and
S.W. Clarke, "Effects of Various Inhalation Modes on
the Deposition of Radioactive Pressurized Aerosols,"
25   European J. Respiratory Dis., Supplement 119,
63:57-65, (1982) demonstrated that the percentage of
aerosol deposited in the lungs of patients was
significantly greater when the patients held their
breath for ten seconds than when breath holding was
30   only four seconds.

Thus, for aerosol to be deposited in the lower
airways, the primary site of action for common medi-
cations such as corticosteroids and bronchodilators,

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the patient must coordinate the release of medica-
tion, inhale slowly enough to minimize loss of medi-
cine through impaction in the throat and upper air-
ways, and breath hold long enough to allow time for
5   small particles to settle. In practice, this means
an inhalation rate below one liter per second, and a
breath hold for up to ten seconds.

A hand-held (e.g., metered or unit-dose)
inhaler currently is a passive device that provides
10   no information regarding the medication actually
delivered. Orehek et al. found that only five of
twenty asthmatic patients correctly inhaled. "The
other 15 patients failed either to inspire deeply or
hold their breath afterwards, or both, or poorly
15   coordinated the puff and the inspiration." Orehek
et al., "Patient Error in Use of Bronchodilator
Metered Aerosols," British Medical Journal, 1:76,
(1976).

For example, it has been found that in a group
20   of 30 acute asthmatic patients directly observed in
a clinical setting, 47% (14 patients) used incorrect
technique. The fourteen patients with inadequate
technique were then trained. Ten of them were
retested after an interval of one day to one month.
25   Five of the patients are still using their inhalers
correctly; the other five had reverted to their
original incorrect techniques. Shim, C., and
M.H. Williams, "The Adequacy of Inhalation of
Aerosol from Canister Nebulizers," The American
30   Journal of Medicine. 69:891-894 (1980).

The device and approach described herein would
have provided immediate feedback to the patients
that they had reverted to incorrect use of their

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inhalers, and provided them with specific guidance
as to what corrective action was required. Thus,
retraining would not have had to wait until their
next visit to the clinic.

5   The present approach also fosters the delivery
of a uniform dose to the target sites of the
patient's lungs upon each inhaler usage with the
expectation of consistent therapeutic response.
Thus, if the patient's symptoms or condition
10   changes, the physician can evaluate the change with
reasonable assurance that the difference is not
simply due to a variation in medication dosage. By
making data regarding the patient's inhaler use
during the entire period between clinic visits
15   available to the physician, therapy can be managed
on a more informed basis.

         It has been observed that, "The lung presents a
significant barrier to the penetration of drug
particles of a size small enough to maximize thera-
20   peutic efficacy." Padfield, J.M., "Principles of
Drug Delivery to the Respiratory Tract", Drug
Delivery to the Respiratory Tract, Ganderton, D.,
and Jones, T., ed., Horwood, London (1987).
Padfield concludes "The design of delivery system
25   for administering drugs to the lung can have as
much, or more, impact as the choice of drug." (id.)
Previous attempts to improve the effectiveness of
aerosol medicine inhalers include a number of
devices including spacers, aerosol holding chambers,
30   flow-activated triggering mechanisms, and dry powder
generators.

         The problem of medicine deposition in the mouth
and throat can be alleviated in some cases by the

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use of a tube spacer, an extension tube inserted
between the metered unit-dose inhaler and he
patient's mouth. This procedure still requires
coordinated patient action and in itself provides no
5   feedback to the patient as to the success or failure
of the overall effort.

Another approach to improving MDI usage is the
use of chambers or reservoirs into which the aerosol
is discharged prior to inhalation. Such devices
10   reduce the need for coordination of actuation and
start of inhalation. A widely used device is
described in Sackner, et. al., U.S. Patent No.
4,484,577, 1984. This device also provides an
audible whistle when the inspiration rate is above a
15   fixed level. The device fails to address inter-
patient variations in correct inhalation patterns,
as well as the breath-holding stage. A common draw-
back of all chamber devices is their bulk. Such
devices may not fit conveniently in a pocket or
20   purse, and many patients are unwilling to use such
large devices due to self-consciousness. The
process in accordance with the present invention can
be used irrespective of whether a tube spacer or a
reservoir is used.

25   Conventional systems also include several
inhaler devices which address the coordination
problem by incorporating a means of triggering the
medication release by the start of inhalation. Such
devices have been described by Wass, U.S. Patent No.
30   4,664,107 1987, and Johnson et. al., U.S. Patent
4,803,978 1989. Shaner, U.S. Patent 4,739,754, 1988
describes a "Suction Resistant Inhaler" whose design
fosters a deep inhalation by the patient.

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Other conventional devices have incorporated electro-mechanical components in order to record the timing and date of usage for review by a healthcare professional. Spector, et. al., "Compliance of
5   Patients with Asthma with an Experimental Aerosolized Medication: Implications for Controlled Clinical Trials," Journal of Allergy & Clinical Immunology, 77:65-70 (1986) discloses the use of a nebulizer chronolog to record the patients usage of
10   MDIs between clinic visits. This incorporates a device for recording the time and date of each canister actuation for later review by physicians conducting research on patterns of patient compliance. This device lacks the capability for
15   obtaining any information regarding the inspiratory maneuver itself. Furthermore, since the intention of the study was to record patients' MDI usage patterns without their knowledge, the device not provide any feedback to the patients regarding
20   proper inhalation technique.

Similar devices are described by Rand et. al., U.S. Patent 4,817,822, 1989, and Dessertine, U.S. Patent 5,020,527, 1991. The Rand device incorpo- rates a mechanical rachet wheel and driving member
25   to drive an indicator of the number of actuations of an aerosol canister. The Dessertine device provides a timer and a counter for tracking the number of and time between actuations.

In the aforementioned devices the time course
30   of air flow is not measured, nor is it compared to the desired pattern for the specific patient as may be determined by a healthcare professional. Thus, these devices address only the aspect of compliance

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relating to if and when the medicine was used.   In
order to assess whether an aerosol medication has
been used effectively, it is necessary to further
determine information regarding the patient's
5   coordination of actuation and inspiration, volume
and flow rate of inspiration, and post-inspiratory
breath holding.

In summary, conventional devices fail to
adequately address the need for immediate patient
10   feedback regarding multiple steps in the correct use
of inhalers.   These devices are also inadequate in
providing information to both patient and healthcare
professional regarding the critical factors which
determine the success of medicine delivery,
15   including coordination of inhalation with actuation,
inhalation flow rate and duration of breath holding.

What is needed is a hand-held inhaler device
which can monitor the complete time course of
airflow during an inhalation, and which possesses
20   the capability to guide the patient in its correct
usage before, during, and after use.   What is also
needed is such an inhaler whose functions include
the capacity to record relevant information about
the timing and nature of its use for subsequent
25   review by a healthcare professional.

SUMMARY OF THE INVENTION

The present device detects how much air is
inhaled through the inhaler with what time course
(including such derived measurements as how much
30   volume is inspired within the bounds of a given flow
range) as well as certain events such as the
triggering of the release of aerosol.   The system

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can be set up to compare the resultant time course
to either (a) a standard target envelope (e.g., one
or more of flow, volume, and time) for that medica-
tion or (b) a specific target envelope for that
5   particular patient programmed into the intelligent
inhalation device by a healthcare professional.
Based on the comparison, the success or failure of
effective inhaler actuation and aerosol inspiration
can be signaled to the patient (e.g., visually or
10   through sound) and may be recorded with a time and
date stamp for later decoding and evaluation by a
suitable healthcare professional. In a preferred
embodiment of the invention, the device would also
possess the ability to signal the patient to
15   continue post-inspiratory breath-holding, and record
the end of breath holding for use in interpreting
the success of medication delivery.

    In addition, immediate feedback can be supplied
to the patient as to the specific nature of any
20   mistakes made. For example, a message might be
given that the patient's inhalation was too rapid.

    In a preferred embodiment of the invention
sufficient memory is provided to store data from a
large number of inhalations. This automated record
25   may be used in conjunction with a manual log kept by
the patient (e.g., what event, such as exposure to
an allergen, caused the need to administer the medi-
cation) or in a semi-automated fashion by having the
patient or attendant encode event-related infor-
30   mation into the inhaler device memory. An example
of the latter would be the pressing of a button in a
certain pattern that would be associated with a

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specific event. This event information could be
stored together with a time and date stamp.

In an alternate embodiment of the invention,
the inhaler device would possess the capability to
5   signal the patient at the times for which its use
has been prescribed. This signal could be provided
by means of indicator light(s), audible beeps or
tones, vibration of the unit, or some combination
thereof. Timing of such signals would be programmed
10 in accordance with standard or patient specific
prescriptions for usage.

In another alternate embodiment of the inven-
tion, the inhaler device would be integrated with a
holding chamber (reservoir) into which the aerosol
15 is released prior to inhalation. The interior
volume of this chamber would be large enough to
allow for the expansion of the aerosol. Electronic
functions remain the same as those provided in the
non-chamber device.

20 BRIEF DESCRIPTION OF DRAWINGS
Figure 1 is an oblique side view of the present
intelligent inhaler device.

Figure 2A is a side sectional view of the
mechanical construction of the device illustrating
25 major components including the incorporation of the
type of pressurized canister most widely used for
dispensing metered doses of aerosols.

Figure 2B is a sectional view of an alternate
mechanical construction incorporating a Venturi-type
30 flow meter.

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Figure 3 illustrates typical messages and graphic output supplied to the patient or attendant by the device.

Figure 4 is a block diagram of electronics illustrating the overall architecture of the intelligent inhaler device

Figures 5A through 5E show the circuit diagrams for subsystems of the device.

Figures 6A and 6B are flow charts showing the overall processes for use of the intelligent inhaler by healthcare professional and patient.

DETAILED DESCRIPTION

The overall process of the present intelligent inhaler system is shown in Figure 6A which provides an overview of the protocol for closing the thera-peutic loop. The target profile envelope is selected and inserted (e.g., via a clinical computer-based workstation). This target envelope is (a) a generic pattern, or (b) a tailored time course based on the patient's individual spirometric values or other input, as appropriate. The device is used by the patient and at the next visit to the physician's office, the utilization data are extracted and transferred to the clinical work-station where they are reviewed by the physician or other healthcare professional including analysis of trends with respect to previous periods. The prescription is adjusted if and as appropriate and, if necessary, a new target profile for the given patient and medication is loaded into the intelli-gent inhaler device.

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Figure 6B is an overview of the process for utilization by the patient. Initially, the device reminds the patient that it is time to take the medication. This is used for medications, such as
5   corticosteroids, which are taken over long periods of time rather than in an immediate reaction to an acute event such as an asthmatic episode. The device is then turned on and the release of aerosol triggered.
10   Recording of data begins at the start of inspiration or upon actuation of the medication canister, whichever is earliest.

The actual time course of each inhalation is compared to the objective target time course, a
15   comparison derived, and a signal given as to success or failure. At the end of inhalation, a timer is started which runs for the period of time during which the patient should hold his or her breath. At the end of ten seconds (or other period as speci-
20   fied), an auditory and/or visual signal is supplied to the patient. The patient can press a button to signal then breath holding actually ended. In an alternate embodiment, he patient can signal that event by exhaling (at least initially) back into the
25   hand-held device with the time recorded when an increase in air flow above a specified threshold is detected.

In addition, suggestions for corrective action (e.g., hold breath for a longer time) can be given.
30   Recorded data are stored for later readout into a record-keeping device (such as a computer-based clinical workstation in a physician's office) for

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interpretation and perhaps comparison to other time
periods by a healthcare professional.

   An external view of the preferred physical
embodiment is shown in Figure 1. Located in the
5   housing 100, is a pressurized medication canister
102. An important feature is the ability to insert
and utilize standard metered-dose inhaler canisters,
although the device can be modified to support other
containers as appropriate. Communication with the
10   patient occurs with input through push-button switch
means 104, and output through LED indicators 106 and
LCD panel display 108. Communication to and from
the clinical workstation in the office of the
physician is through input/output data communication
15   means 221 as shown in Figure 2. While this is shown
as a simple 1/0 data connector socket in Figure 1,
the invention is not so limited. The data communi-
cation means 221 in Figure 2A also is intended to
include a compact transceiver means for communi-
20   cating with a spatially remote control source, such
as a workstation, through a radiofrequency communi-
cation channel, or the like in accordance with well
known techniques. The remote workstation is capable
of receiving transmission of data such as the time
25   of actual usage or the inhalation pattern. The
present device is also capable of being reprogrammed
by the remote workstation to alter the dosage or to
provide specific feedback to the patient as to
corrective action.
30   Air to be mixed with the aerosolized medication
enters from the opening in the top of the inhaler
housing 112, and the patient's inspiration pulls the
air and aerosol mixture through mouthpiece .114.

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A mechanical construction diagram of a
preferred embodiment of the device is shown in
Figure 2A. The "on" switch 104 for the device turns
on the power in the battery 205 (which is physically
5   accessible through cover 207) for circuits which are
not active between times of inhaler usage. Other
circuits may be powered at predetermined times, and
power is supplied continuously to circuits
responsible for maintaining the contents of memory.
10   The Application Specific Integrated Circuit (ASIC)
220 contains the microprocessor, memory, calendar/-
clock, power controller, LED/sound driver, LCD
driver, input/output interface, button-switch inter-
face, and analog to digital converter. The elec-
15   tronics are connectable to a workstation by a
conventional connector means 221. Whether the
device has been shaken properly is determined by
input from motion sensor 222. Flow is measured
utilizing a flow measuring means or flow meter
20   (comprised of elements 232, 230, 234 and 112) as
follows. Differential pressure is measured through
pressure sensor diaphragm 230 which is connected by
flow channels 232 to both outside atmosphere and
interior flow chamber 234. Pressure-sensor dia-
25   phragm 230 is connected to the pressure-sensor elec-
tronics 240 which are interfaced to an analog to
digital converter on ASIC 220. Aerosolized
medicament is released when the medication canister
102 is depressed and its valve 203 is opened with
30   the pressurized liquid being discharged through the
atomizer 242. An actuation pressure switch 244 is
disposed for contact with canister 102 when the

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canister is depressed to discharge a unit of
medicine through atomizer 242.

Figure 2B illustrates an alternative embodiment
utilizing a venturi flow meter design. This
5   construction is the same as in Figure 2A except that
the linear response of pressure sensor diaphragm 230
is proportional to flow through the Venturi-flow
meter 250, with the signal transmitted by the
pressure sensor electronics 240. This implementa-
10   tion provides the ability for the patient to exhale
(at least initially) into the device to indicate he
end of the breath-holding period. The exhalation
would be into he input port 112 to avoid clogging
the atomizer 242. This port 112 could be used for
15   recording the patient's maximal exhalation or other
spirometric measurements. The form of pressure
sensor is not critical. A semiconductor pressure
sensor might be directly "incorporated into an ASIC
device [Wise, K.D., and K. Najafi, "Microfabrication
20   Techniques for Integrated Sensors and Microsystems,"
Science, 254:13351342, (1991)]. Alternatively, a
different means for measuring air flow such as a
miniaturized mass flow sensor, could be employed.

Figure 3 shows a set of sample messages to the
25   patient. Feedback regarding individual inhalation
efforts appears in the left column, including an
illustration of the time course of inspiration rela-
tive to a target range. General instructions are
shown in the center, and prompts for event recording
30   are shown on the right. These messages are
displayed by the LCD panel 108 as shown in Figure 1.
Auditory output comes through the Piezo sound
generator 260 as shown in Figure 2A and 2B.

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Figure 4 shows a block diagram of the system.
In a preferred embodiment, many of the electronic
elements are incorporated within application
specific integrated circuit (ASIC) 220, including
5   the microprocessor, RAM and ROM storage, calendar/-
clock, A/D converter, 1/0 functions, and drivers for
LCD, sound, and LED devices. However, in various
implementations of the invention these functions may
be distributed on multiple integrated circuits,
10   including standard and/or custom devices. The scope
of the invention is not limited to any single
specific implementation.

The microprocessor memory requirements are
supplied by the Random-Access Memory (RAM) and the
15   Read-Only Memory (ROM) modules. The calendar/clock
module provides the ability to signal to the patient
when it is time to take the medication, and gener-
ates time and date stamps for each inhaler use. The
analog input signal from the pressure-sensor elec-
20   tronics is transformed by the analog to digital
converter. The power controller provides power to
all the device subsystems including the micro-
processor and associated components, flow-measuring
circuit, LED/sound display and driver, ind the LCD
25   alphanumeric panel and driver. Input/output
circuitry handles signals coming into and/or going
out of the push-button contact switches and two-way
communications with the computer-based clinical
workstation or other suitable device occurs through
30   the external communications connector 221.

Figures 5A through 5B illustrate subsystem
circuit diagrams. Figure 5A shows the power control
circuit. Modules such as the PAM are powered

continually. As to power control, when the motion
sensor 500 is triggered with transmission through
the MOSFET semiconductor 502 on the left or the "on"
504 button switch closed, the NAND 508a, 508b gates
5   change state and switch on the MOSFET semiconductor
510 on the right to provide voltage to the micro-
processor. When the microprocessor goes into the
"sleep mode" after its operational sequence, it
transmits an "off" signal to the MOSFET semi-
10   conductor 512 which deactivates the NAND gates 508a,
508b and shuts the system down. The device is
battery operated using preferably a lithium battery
for long life.

        Figure 5B shows the pressure-sensor flowmeter
15   electronics. The strain gauge resistors 520a, 520b,
520c and 520d in the bridge circuit are located on
the pressure-sensor diaphragm 230 which measures the
pressure differential in the flow meter comprised of
elements 232, 230, 234 and 112 in Figure 2A or in
20   the Venturi flow meter 250 shown in Figure 2B. In
accordance with techniques which are well known to
those skilled in the art, an analog signal is
generated through the two stages of operational
amplifiers 522, 524. This signal is transformed by
25   the analog-to-digital converter 530 and fed via a
bus to the microprocessor (not shown).

        Figure 5C illustrates the LED/sound display and
driver. The control signal comes from the micro-
processor to 8 bit latch 540. The control signal is
30   stored by the 8-bit latch 540. Selected components,
such as zero to six of the LEDs 542 and zero to two
Piezo sound generators 544 are turned on. In like
manner, components which are on can be turned off

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with a subsequent control signal transmitted by the
microprocessor.

     Figure 5D presents the block diagram for the
LCD alphanumeric panel and driver. The control
5   signal comes in over the bus to the microprocessor
and the LCD controller provides input to the LCD
driver (input to rows of display) and the LCD dot-
matrix display panel (input to columns of display)
in accordance with techniques which are well known.

10   Figure 5E illustrates the push-button switch
interface. Because this interface resides on the
microprocessor bus, a three state buffer is used
(off, floating, on). In the figure, the term
tristate is used, reflecting a particular version of
15   the buffer produced by National Semiconductor Corpo-
ration. The current status of each of the push-
button switches is held within the buffer. The
three-state buffer is interrogated by the micro-
processor by turning the three state control to "on"
20   and the status of each line ("on" or "off") is
transmitted from the three-state buffer back to the
microprocessor over the microprocessor bus.

     Figure 6A shows the overall protocol whereby
data collected by the intelligent inhaler are used
25   to close the therapeutic loop, and enable the
healthcare provider to track the patient's medica-
tion use between visits. The physician selects the
target profile for the patient and medication. The
profile is loaded into the device and the device is
30   used by the patient. At the next visit of the
patient to the healthcare provider, the data related
to patient utilization of the device is extracted
and moved to the clinical workstation. The data are

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then reviewed by the physician and trend analysis
can be done, not only within the given set of data,
but in comparison to previous periods. An adjust-
ment can be made to the prescription if the
5   physician chooses to do so. If there is a change,
the new prescription information and/or target
profile are loaded into the intelligent inhaler
device.

Figure 6B illustrates the process of utiliza-
10   tion of the intelligent inhalation device by the
patient. If the medication is taken at prescribed
intervals rather than on an episodic basis, a
reminder of the time to take the medicine is
signalled to the patient. The patient depresses the
15   "on" switch to indicate the medicating sequence is
to be started and shakes the device with the
canister inserted so the medication is adequately
prepared for discharge. Depression of the canister
enough to discharge the medication is the trigger
20   event. Recording of the data, including release of
aerosol, airflow time course, and associated time
and data stamps ensues. Derived values are calcu-
lated and compared to the target values of the
target function. The breath holding period is timed
25   and an auditory and/or visual signal supplied to the
patient at its end. Auditory and/or visual feedback
is provided to the patient as to success or failure
of the inhalation actions including text messages as
to what corrections are appropriate (e.g., INHALE
30   SLOWER). At the next patient visit, the recorded
data are read into the host clinical workstation and
the data analyzed and displayed, including trend
analysis in comparison to previous periods.

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A typical cycle of operation, with reference to Figures 1, 2A and 2B, is as follows:

If the medication is to be taken regularly, the time for the medication to be taken can be signalled
5   through Piezo sound generator 260 and/or LED display 108.

The unit is held in patient's hand such that mouthpiece 114 faces the patient.

The patient presses push-button switch 104,
10   activating the "on" switch to close and activate the microprocessor and associated functions.

The patient shakes the unit per instructions, causing the motion sensor 222 to generate a signal for storage in the memory contained in the ASIC 220.
15   If the on switch 104 has not yet been activated, motion sensor 222 causes the unit to turn on just as if the on had been closed. Optionally, this signal also prompts indicator lights 106 to turn on as well.

20   Patient then places the mouthpiece 114 in mouth, depresses medication canister 102 firmly enough to cause metering mechanism 203 to discharge a unit of medicine through atomizer 242, and the patient simultaneously begins to inhale. Depression
25   of the canister 102 causes closure of actuation sensing switch 244 and transmission of a signal for this event to microprocessor within the control electronics of ASIC 220.

With the inhalation, aerosolized medication
30   flows through the mouthpiece 114 into the mouth of the patient.

Pressure-sensor diaphragm 230 senses air flow coming through the upper housing opening 112 and

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moving through flow chamber 234 by measuring the
pressure differential between the outside air
through passage 232 and the internal chamber 234 (in
the configuration shown in Fig. 2A). In the alter-
5   nate construction shown in Figure 28, pressure
sensor diaphragm 230 senses air flow by measuring
the pressure differential between the two stages of
Venturi flow meter 250. Pressure-sensor electronics
240 generates a signal representative of flow rate
10   to the analog-to-digital converter contained in the
ASIC 220.

The analog-to-digital circuitry converts this
signal to digital form, upon which it is stored as a
series of (e.g., 8-bit) samples in a RAM contained
15   in the ASIC 220.

As patient continues to inspire, time series
flow samples in memory are compared with target
objective profile representative of correct inhala-
tion technique also stored in RAM contained in ASIC
20   220. The microprocessor contained in ASIC 220
performs the comparison of actual versus target
values and depending upon the results sends signals
to indicator LED's 106.

Upon completion of inspiration, cessation of
25   flow is detected and measurement of time duration of
breath hold begins using the calendar/clock module
contained in ASIC 220.

Upon end of breath hold, patient presses push
button 104 which sends an event signal to micro-
30   processor in ASIC 220 for storage in PAM and calcu-
lation of breath-holding duration.

Results of the maneuver, including breath
holding performance are used to select textual or

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iconic feedback from a table stored in RAM contained
in ASIC 220, in accordance with techniques which are
well known for display to patient via LCD display
panel 108. Note that text table can consist of
5   multiple sections corresponding to differing
languages.

After the inhalation maneuver is complete, the
device can pose questions to the patient on LCD
display 108 and answers such as "yes" or "no", or
10   other answers corresponding to the number of times
the push button switch is activated are input by the
patient through push-button switch 104.

After a specified time (long enough to permit
an additional discharge of medication if there is to
15   be one) an output signal from the microprocessor to
the power control circuit causes the system to
return to sleep mode.

Data from multiple maneuvers can be downloaded
subsequently through connector 221 into a clinical
20   workstation or similar device for review by profes-
sional including trend analysis within the set of
just downloaded data and comparison to previous
periods.

Upon downloading of data, records for
25   individual maneuvers are erased from the RAM
contained in ASIC 220, and battery 205 is checked
for charge.

The site of compliance monitoring includes a
digital computer means (not shown) for communicating
30   electronically with the microprocessor means 220
incorporated in the programmable inhaler. The
digital computer means at the monitoring site
includes means for monitoring and improving a

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patient's medication compliance with the use of the
hand-held inhaler. The monitoring computer is
linked with transmission means for remote electronic
retrieval of the data measured by and stored in the
5   inhaler microprocessor through data communication
techniques which are well known, such as radio-
frequency, optoelectronic communication, or the
like.

The monitoring computer is programmed to
10   evaluate the data received from the inhaler micro-
processor means and to provide interpretations of
the effectiveness of compliance efforts based on he
retrieved data. The monitoring computer also
includes a display means for meaningful display of
15   the compliance data. Such display means preferably
includes patient's projected target envelope for
maximized delivery of medication as compared to the
actual, measured performance of the patient.

It will be appreciated by those skilled in the
20   art that there are a multitude of methods for
programming the monitoring computer to achieve the
evaluation of a patient's medication compliance
parameters which will maximize delivery of medica-
tion to the large airways, small airways, alveoli or
25   any part of the respiratory tract. Thus, the
present method is not intended to be limited to a
specific software implementation for diagnosing a
patient's projected compliance as a target envelope
of values and for measuring the actual performance
30   of the patient with respect to the target envelope.

In a preferred embodiment, the monitoring
computer includes software which is readily
programmed by one skilled in the art to utilize data

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input from diagnostic instruments, diagnostic tests,
clinical records, clinical observations, profes-
sional opinions, or the like in calculating a target
envelope of inhalation parameters which will maxi-
5   mize the delivery of aerosolized medication to any
selected part(s) of the respiratory tract of a
particular patient, or to indicate other changes in
therapy such as type of medication. The foregoing
data include quantifiable parameters relating to the
10   physical condition of the airways of a patient, such
as the size of the patient's air passages.

The data are input into the monitoring computer
as a table of values, or physical parameters indica-
tive of the condition and capacity of a patient's
15   air passageways and inhalation characteristics. The
table of physical parameters are then mapped to
provide the target envelope of values, which if
matched by the patient's performance, will maximize
the distribution of the aerosol medication any
20   selected parts of the respiratory tract. The moni-
toring computer compares the patient's actual
measured performance to the target envelope. The
monitoring computer then communicates electronically
with the microprocessor in the inhaler, ind as a
25   function of measured compliance parameters, repro-
grams the microprocessor, if necessary, with differ-
ent target inhalation profiles, dosage levels or
actuation event times that will bring the patient's
performance within the target envelope and maximize
30   the therapeutic response.

The advantages of the system described herein
over conventional devices may be summarized as
follows:

(a) the incorporation of both monitoring and
recording the patient's inhalation time course and
related events in a medicine inhaler device small
and aesthetically pleasing enough to be used during
5 normal day-to-day activities,

(b) the ability to load in a target perfor-
mance envelope for one or more inhalation time/value
courses and/or one or more selected variables (such
as peak-flow rate) or to designate a specified
10 generic curve,

(c) the ability to sense whether the device
has been shaken properly prior to discharge of a
dose of aerosol,

(d) the ability to provide immediate feedback
15 both during the inhalation and afterwards as to
where the patient's performance fits relative to the
target-performance envelope and whether and when
inhalation values fell outside that envelope,

(e) the ability to provide feedback to the
20 patient as to what corrective action, if any, should
be taken,

(f) the ability to provide a signal to the
patient prompting him or her to continue breath
holding,

25 (g) the ability to have the patient record the
timing of the end of the breath-holding period,

(h) the ability to store any of the data
obtained,

(i) the ability to download longitudinal
30 results from the Intelligent Inhaler into a health-
care workstation or similar device, and

(j) the ability for the healthcare profes-
sional to review a patient's medicine usage for the

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entire period between office visits, and therefore
review trends in the patient's condition in the
context of a detailed historical record of the
actual delivery of medication to its target sites of
5   action in the lungs.

It should be noted that all of the above capa-
bilities would not necessarily be included in every
implementation of the system.

The device and method described here are not
10   limited to usage with any one pharmaceutical. They
may be used with locally acting respiratory drugs
including bronchodilators, corticosteroids, anticho-
linergics, antibiotics, and others, as well as with
systemically acting drugs. Differing compounds may
15   require variations in prescribed usage, including
changes in the inspiratory flow pattern. Such
patterns may be chosen in order to direct the
concentration of drug deposition at different sites
within the respiratory tract, or compensate for
20   variations in patient's airways morphology due to
disease or trauma.

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WHAT IS CLAIMED IS:

    1.   A hand-held inhaler device comprising:

    delivery means for delivering a desired unit dose of aerosolized medication from an associated canister;

    electronic sensor means for continuous measurement of air flow through said medication delivery means;

    means for storage of data including relative time of device actuation of said delivery means, and data representative of duration of inspiration through said medication delivery means.

    2.   The device of claim in 1 further comprising:

    means for performing logical operations or interpretive calculations upon said data;

    signaling means, responsive to said means for performing, for providing feedback to a user, wherein said feedback expresses to a user whether the medicine delivery means has been used correctly.

    3.   The device of claim 2 wherein said signaling means includes means for signaling to a user the scheduled time for activating said medication delivery means.

    4.   The device of claim in 1 further comprising:

    means associated with said means for storage of data for retaining recorded data from multiple delivery activation events;

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means for later retrieval of said data for review by a healthcare professional.

5.   A device according to claims 1 and 2, wherein a target envelope pattern representing the time course of an effective inspiration is stored in the device for comparison to actual inspiration patterns, whereby such comparison is used to govern feedback supplied.

6.   A device according to claim 2 wherein feedback to the user includes specific advice in the form of textual messages and/or labeled indicator lights as to the type of corrective action necessary for effective use of device.

7.   A device according to claim 2 wherein said means for performing logical operations further comprises a means for recording timing of the end of a post-inspiratory breath-hold period.

8.   An apparatus according to claim 2 wherein said means for performing logical operations further comprises a motion sensor means for detecting if said medicine canister is shaken prior to each actuation.

9.   An apparatus according to claim 1 wherein said means for delivering includes a mouthpiece having a mouthpiece cover which upon rotation or removal activates the electronic functions.

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10. A device according to claim 2 wherein the means for performing logical operations further comprises the ability to make spirometric measurements.

5   11. A programmable hand-held medicine inhaler for delivering a predetermined unit dose of aerosolized medication comprising:
        a means for storing a quantity of aerosolized medicine;
10   a means for delivering a desired aerosolized dosage of said medicine into the mouth of said patient;
        a means responsive to a remotely generated input signal indicative of the times prescribed for
15   delivery of said dosage of medicine, wherein said means for indicating comprises at least one of the following: indicator lights, auditory tones and vibration.

        12. An apparatus according to claim 11 further
20   comprising means for generating and storing in memory an activation record of data relating to the effective delivery of said dosage of medicine to a patient.

        13. An apparatus according to claim 11 wherein
25   said means for storing comprises a reservoir of aerosolized medicine integral with said hand-held inhaler.

        14. An apparatus according to claim 11 wherein said means for storing comprises a reservoir of

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aerosolized medication external to said hand-held
inhaler including conduit means for communicating
said aerosolized medication with said hand-held
inhaler.

5   15.   An apparatus according to claim 11 wherein
said means for delivering further comprises a spacer
integral with said hand-held inhaler and interposed
between said hand-held inhaler and the mouth of
patient.

10   16.   An apparatus according to claim 11 wherein
said means for delivering further comprises a spacer
separated from said hand-held inhaler and communi-
cating therewith through a conduit means, said
spacer being interposed between said hand-held
15   inhaler and a patient for delivering said desired
aerosolized dosage of medicine into the patient's
mouth.

17.   An apparatus according to claim 11 further
comprising data communication means for transmitting
20   said data relating to the effective delivery of
aerosol medication to a spatially remote control
means.

18.   An apparatus according to claim 11 further
comprising reception means responsive to remotely
25   generated control signals for enabling said inhaler
device to be reprogrammed to change times
characteristics.

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19.   A programmable hand-held medicine inhaler
for delivering a desired aerosolized dosage of
medicine into the mouth of a patient comprising a
built-in timer means for notifying a patient when to
5   take said medicine.

20.   A digital computer implemented method for
monitoring and improving a patient's medication
compliance with a programmable hand-held medicine
inhaler, comprising the steps of:
10   (a)   measuring the time, date, and
inspiration pattern in said patient's use of a
medicine inhaler;
               (b)   storing the measured values in a
microprocessor means incorporated in said inhaler;
15   (c)   retrieving said values into a display
unit of a computer monitoring means;
               (d)   visually displaying said values on
said display unit to permit compliance monitoring;
       21.   The method of claim 20 wherein the step of
20   visually displaying includes the step of further
processing of selected spirometric measured values
in a computer means to provide feedback of a
patient's therapeutic response.

       22.   The method of claim 21 wherein said step
25   of further processing includes the step of
displaying a target inspiration pattern on said
display unit as a function of time.

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23. The method of claim 22 wherein said step of further processing includes the step of displaying a comparison of a patient's actual inhalation pattern with a prescribed target pattern.

5   24. The method of claim 23 wherein said stop of further processing includes the step of displaying recommendations regarding changes in the patient's inhalation technique.

25. The method of claim 21 wherein said step
10   of further processing of values includes the steps of retrieving said values at a location spatially remote from the site of compliance monitoring, and electronically transmitting said values to said computer monitoring means at said monitoring site.

15   26. The method of claim 20 including the step of transmitting electronically prescribed inhalation pattern dosage from a remote location to reprogram the microprocessor means incorporated in said inhaler device.

20   27. A medicine-compliance monitoring system comprising:
       a programmable hand-held medicine inhaler means for measuring and recording data regarding usage of said inhaler;
25   a digital computer means including a display means for displaying said recorded data;
       transmission means for remotely retrieving said data from said programmable inhaler means and for storing said data in said digital computer

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means, whereby said data is selectively displayed by said display means.

28. The system as in claim 27 wherein said digital computer includes means for evaluating the
5   effectiveness of compliance efforts based on said retrieved data and displays changes in a patient's prescription and therapeutic plan.

29. The system as in claim 28 wherein said means for evaluating includes means for processing
10   data input from at least one of the following sources:

diagnostic instruments, diagnostic tests, clinical records, clinical observations, and professional opinions.

15   30. A programmable hand-held inhaler for dispensing a predetermined quantity of medication to a patient comprising:

a body; a means for containing a quantity of aerosolized medication having a connection with
20   said body;

means provided in said body for delivering, upon activation, a predetermined amount of said aerosolized medication into a mouthpiece to be inhaled by said patient;
25   digital computer means provided in said body being programmable for dispensing medication in a predetermined amount and at selected times, said computer means including means for measuring parameters indicating optimal delivery of said medication
30   from said mouthpiece to said patient;

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said digital computer means further
including means for storing an activation record of
said measured parameters for each activation of said
inhaler;

5   display means provided on said inhaler
body and responsive to said digital computer means
for providing a visual display of the measured
results of an activation event; and

           monitoring means communicating electronic-
10   ally with said inhaler for retrieving and processing
said stored activation data and for reprogramming
said digital computer means as a function of said
measured parameters to maximize delivery of medica-
tion to said patient.
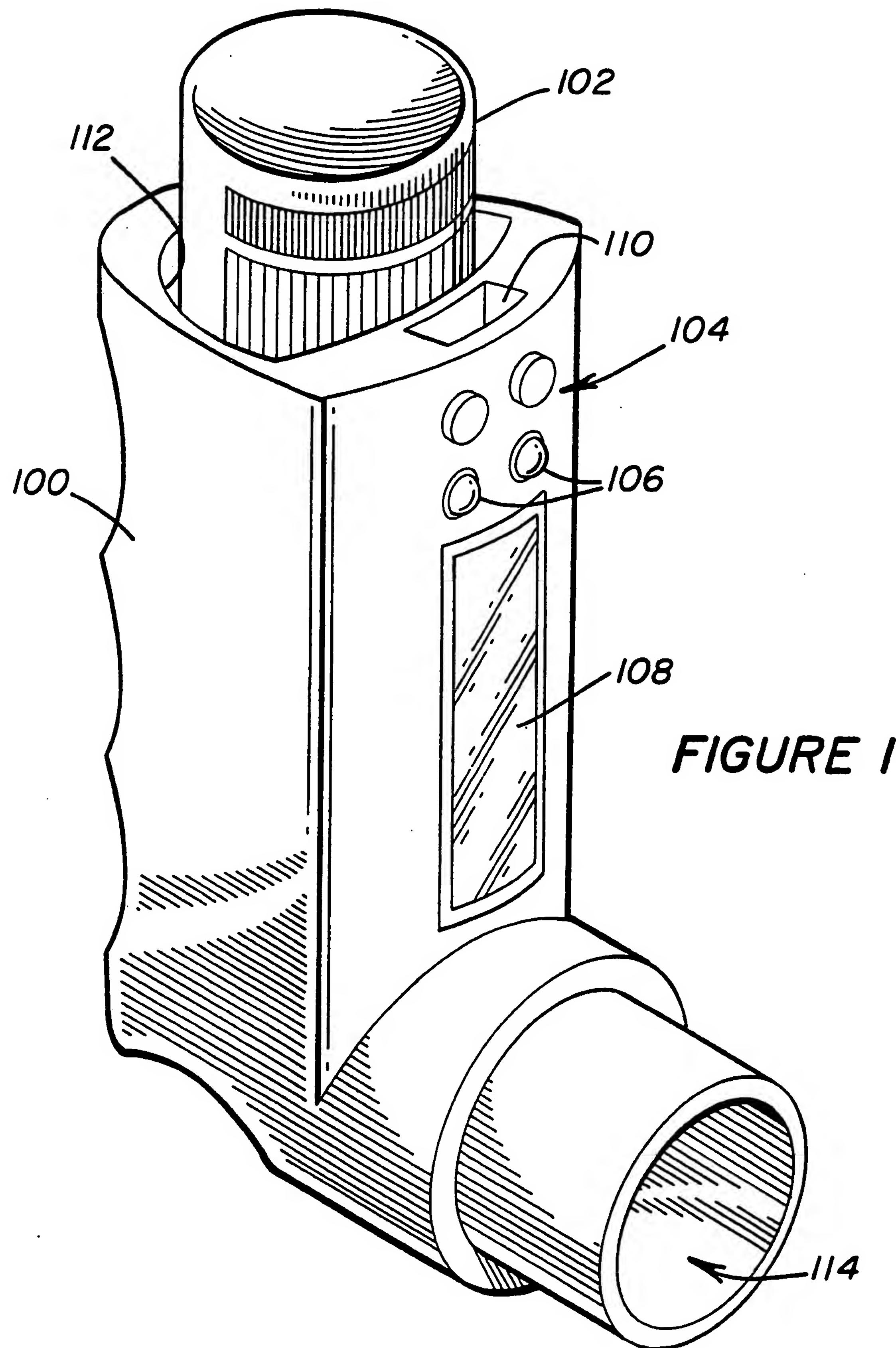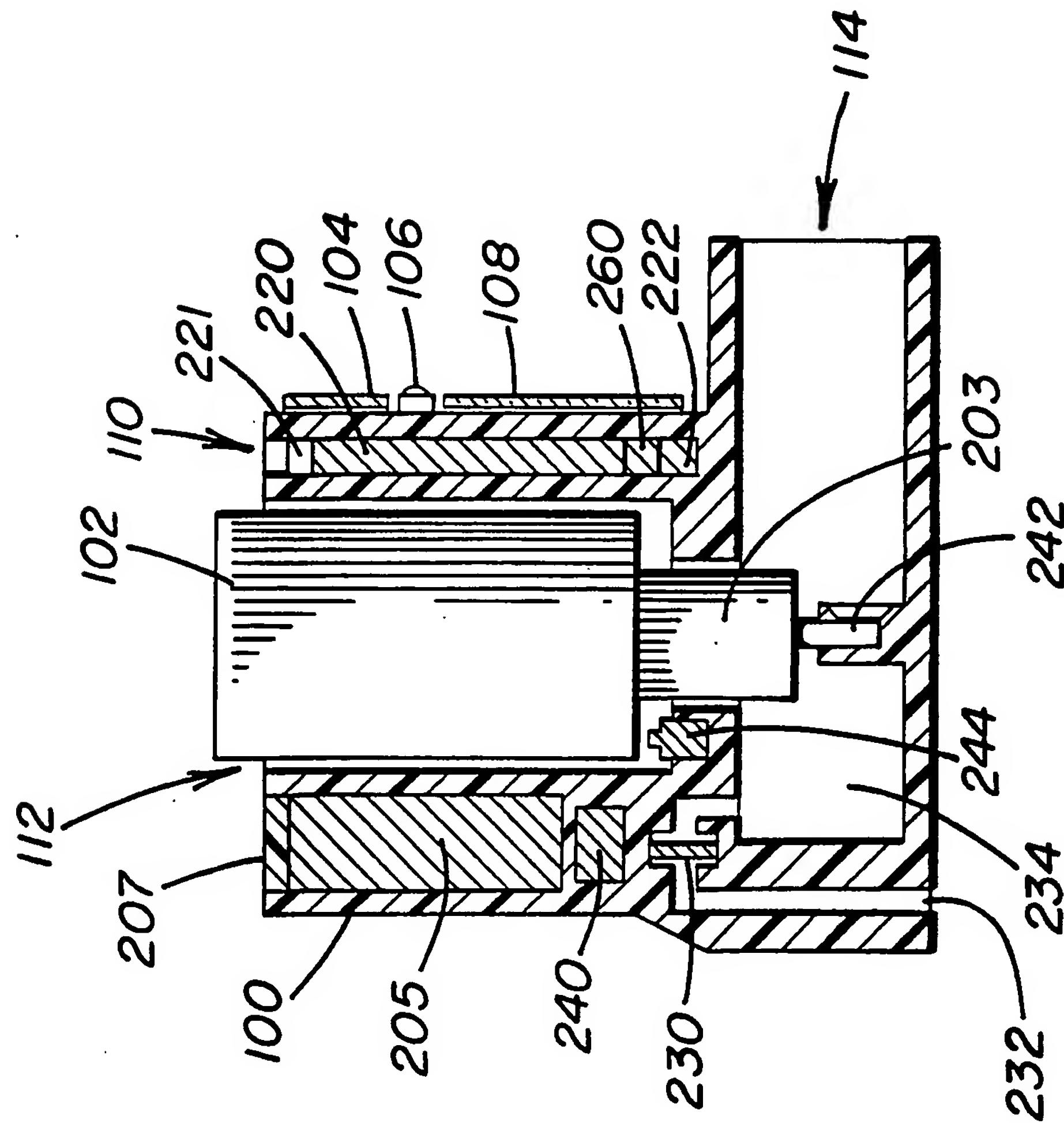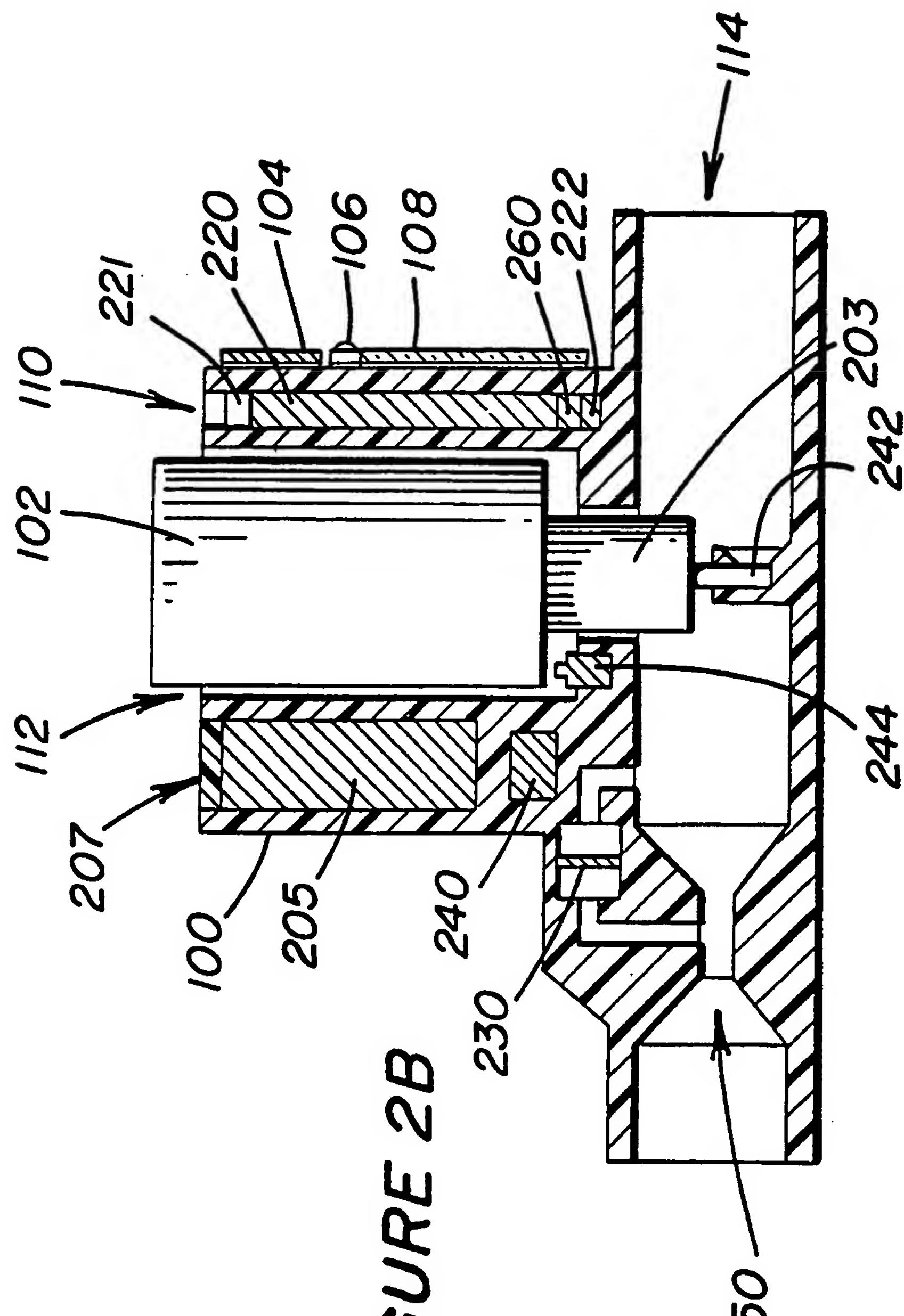
FIGURE I

FIGURE 2A

FIGURE 2B

SAMPLE MESSAGES

ALLERGEN EXPOSURE

IRRITANT EXPOSURE

COLD AIR EXPOSURE

EXERCISE

SHAKE INHALER

READY

RINSE OUT MOUTH

ONE MORE PUFF

TWO MORE PUFFS

HOLD BREATH LONGER

INHALE MORE SLOWLY

INHALE LONGER

INHALE MORE SLOWLY
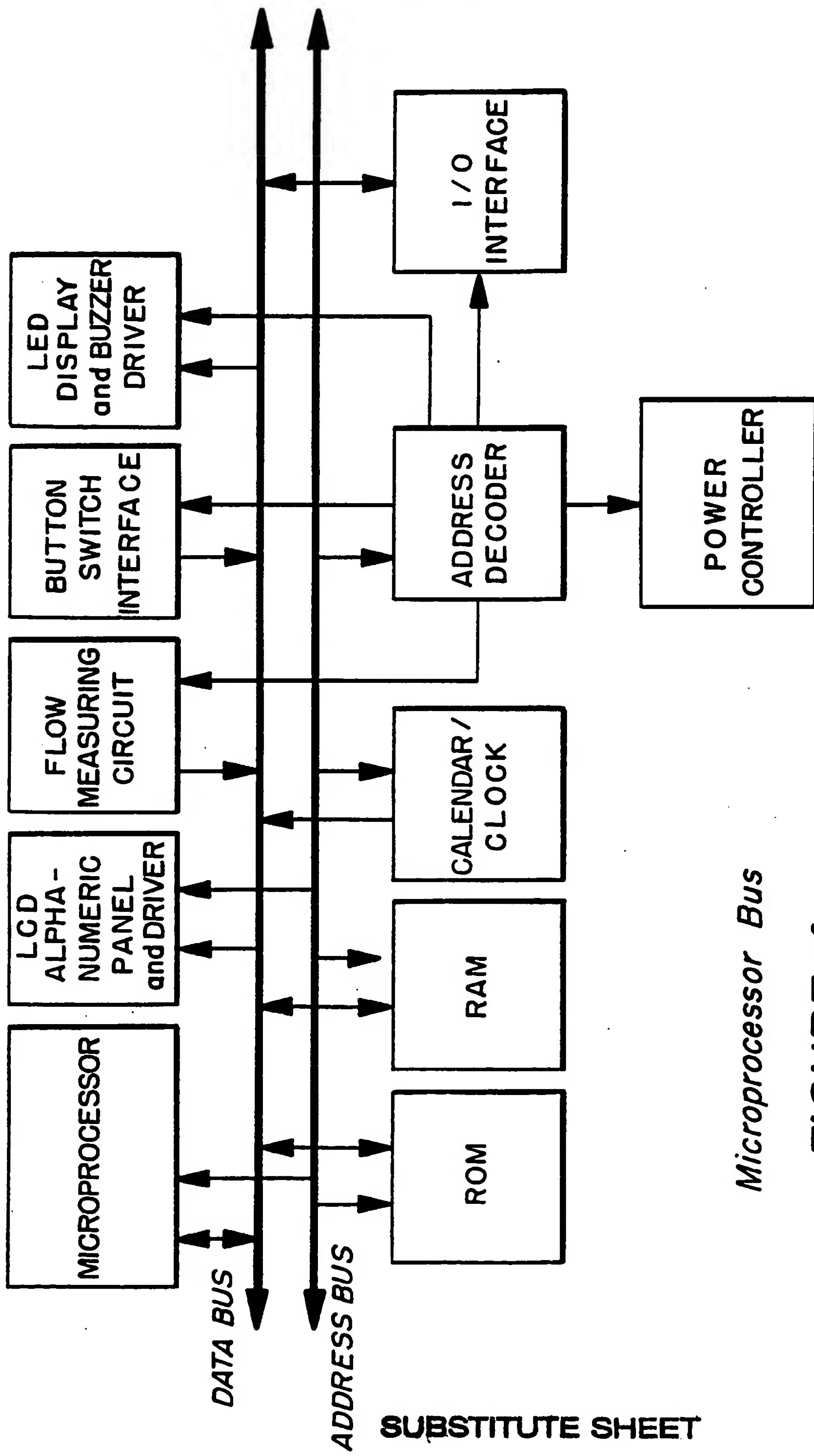
FIGURE 3

Microprocessor Bus
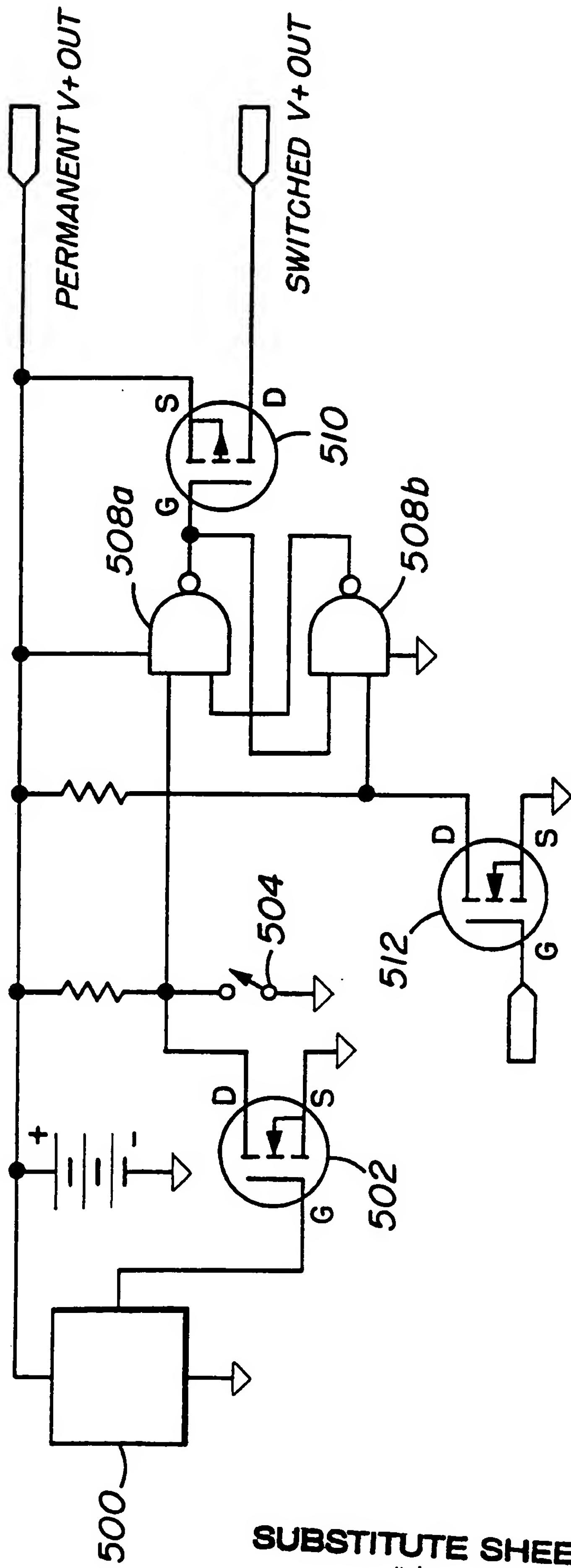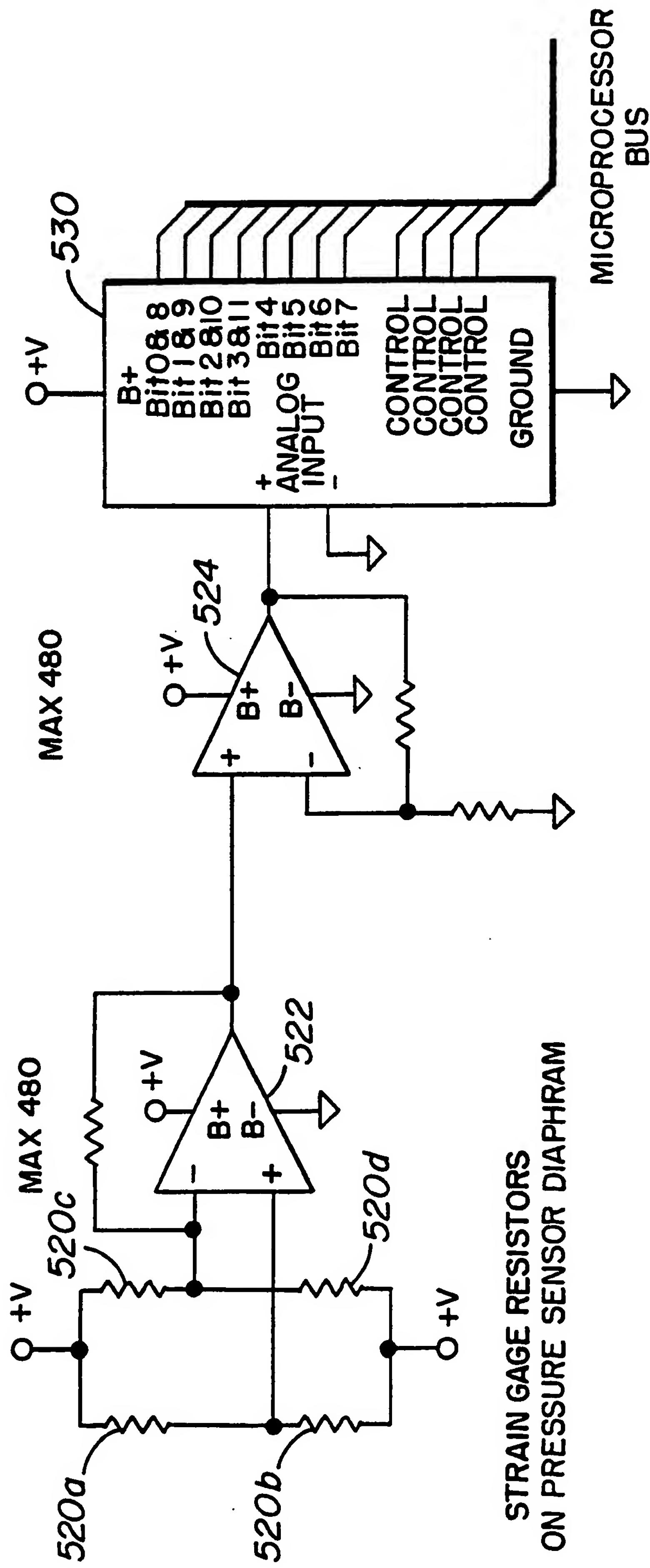
FIGURE 4

FIGURE 5A

FIGURE 5B

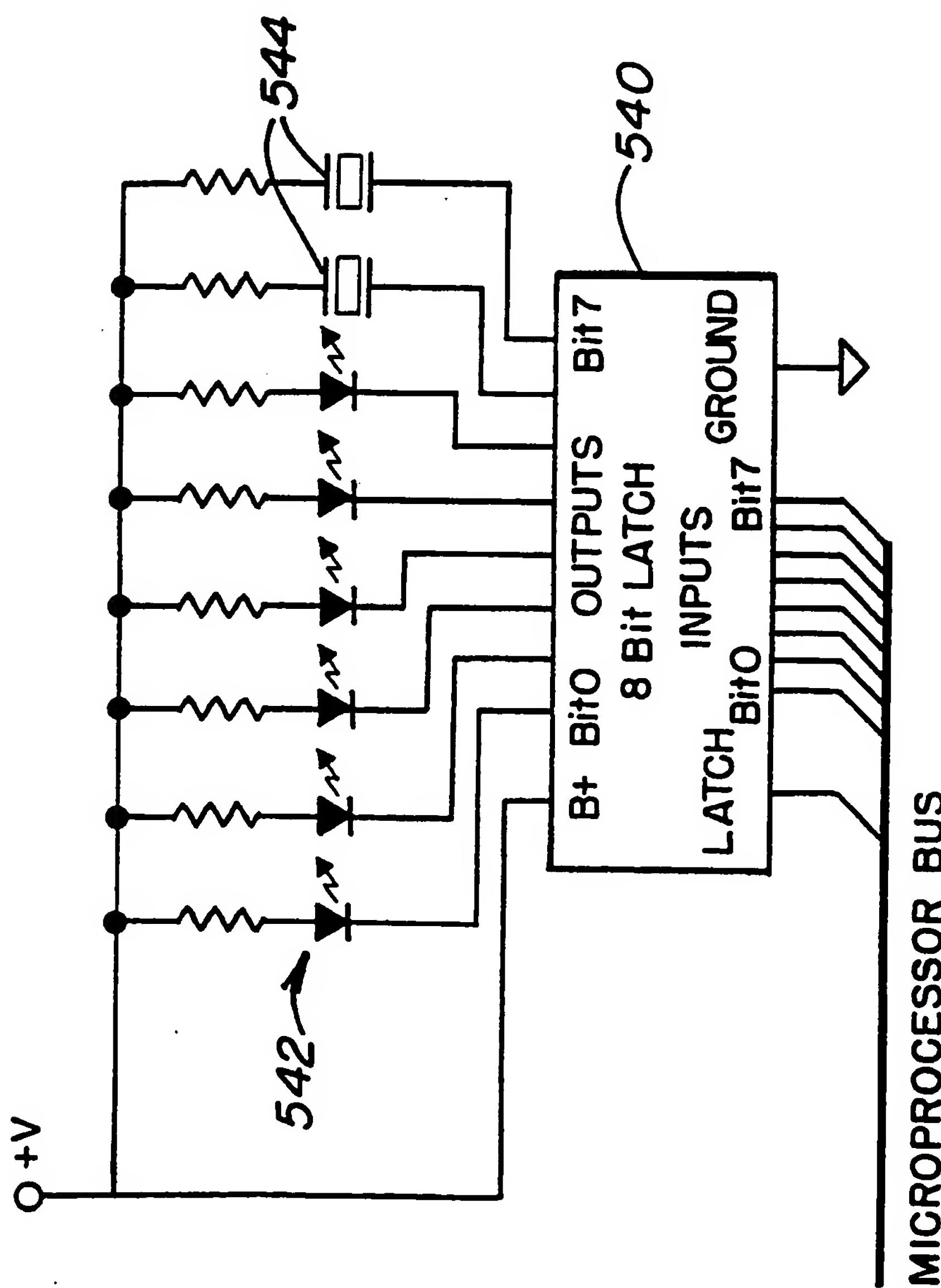FIGURE 5C

LED DISPLAY and BEEPER DRIVER

FIGURE 5D

FIGURE 5E

ADJUSTMENT OF PRESCRIPTION
AS APPROPRIATE

SELECT TARGET PROFILE FOR
PATIENT AND MEDICATION
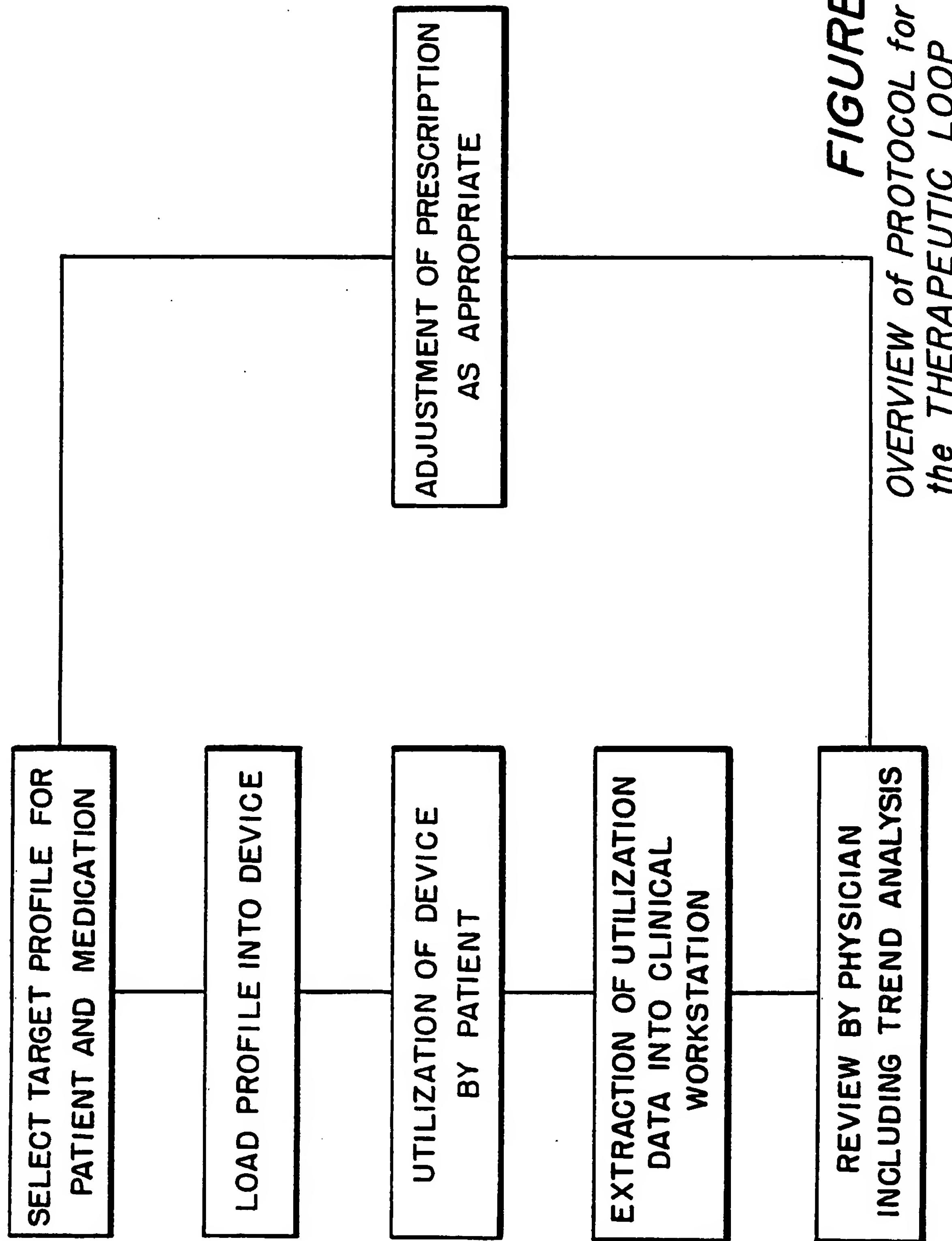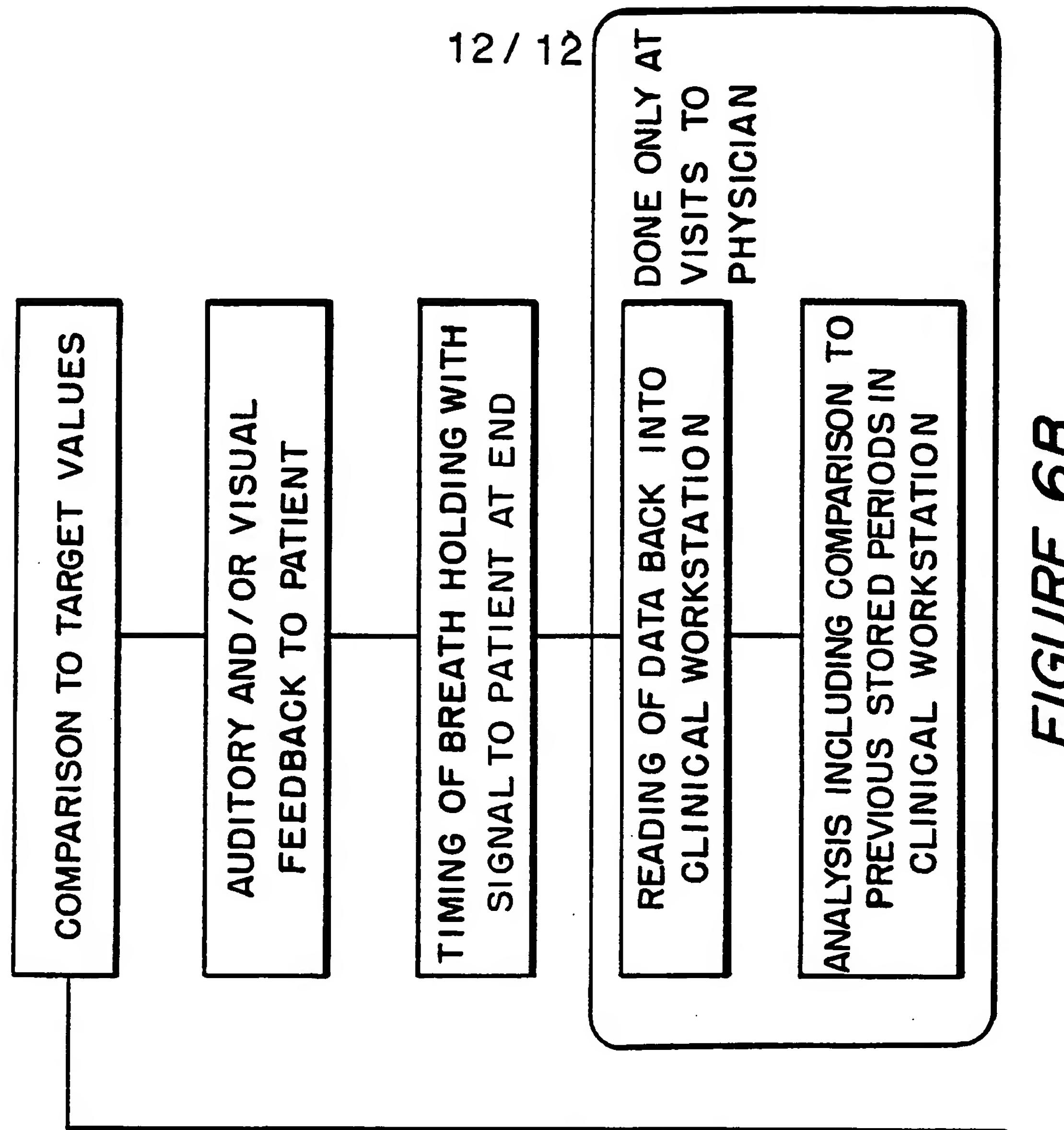
LOAD PROFILE INTO DEVICE

UTILIZATION OF DEVICE
BY PATIENT

EXTRACTION OF UTILIZATION
DATA INTO CLINICAL
WORKSTATION

REVIEW BY PHYSICIAN
INCLUDING TREND ANALYSIS
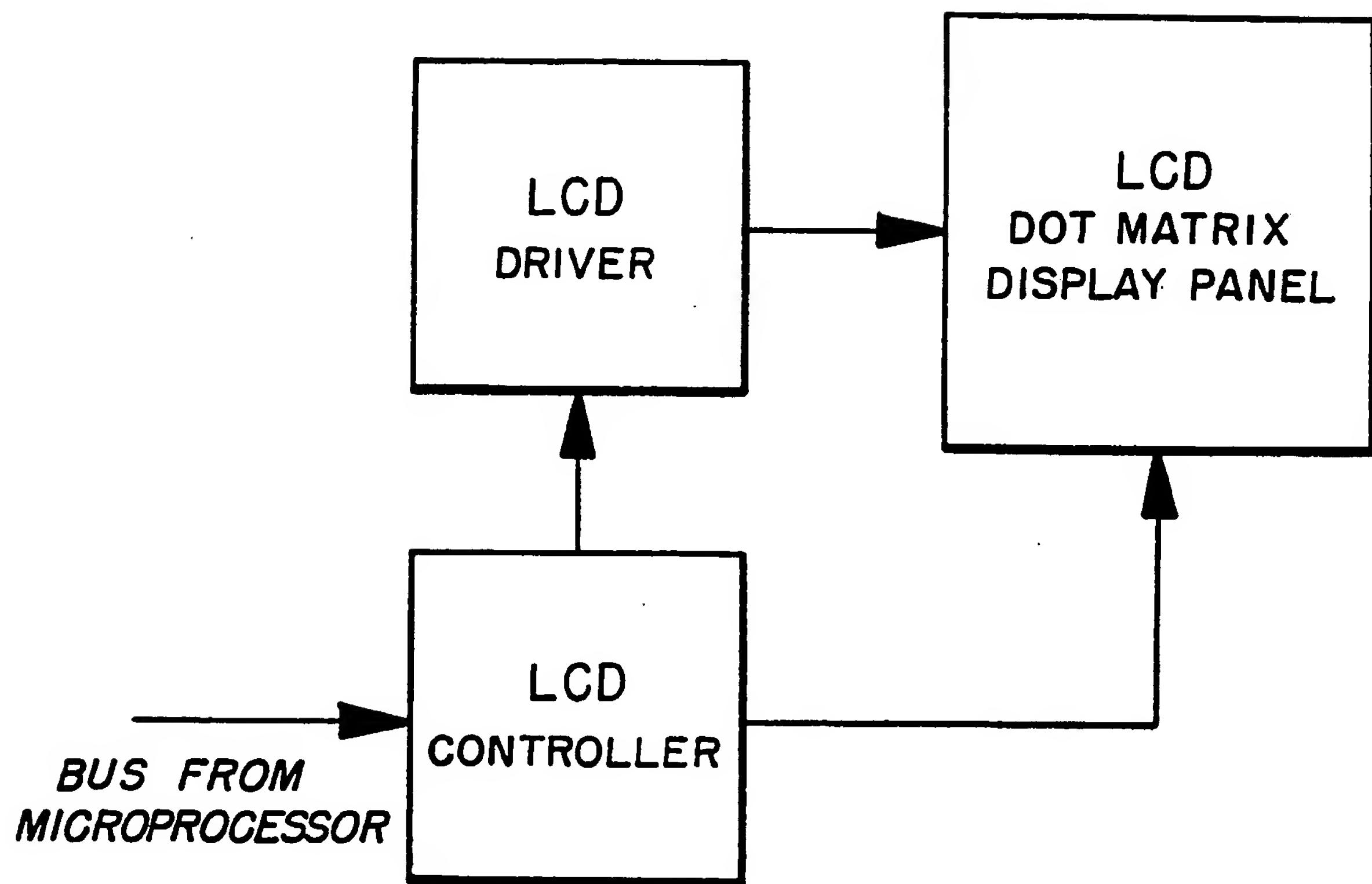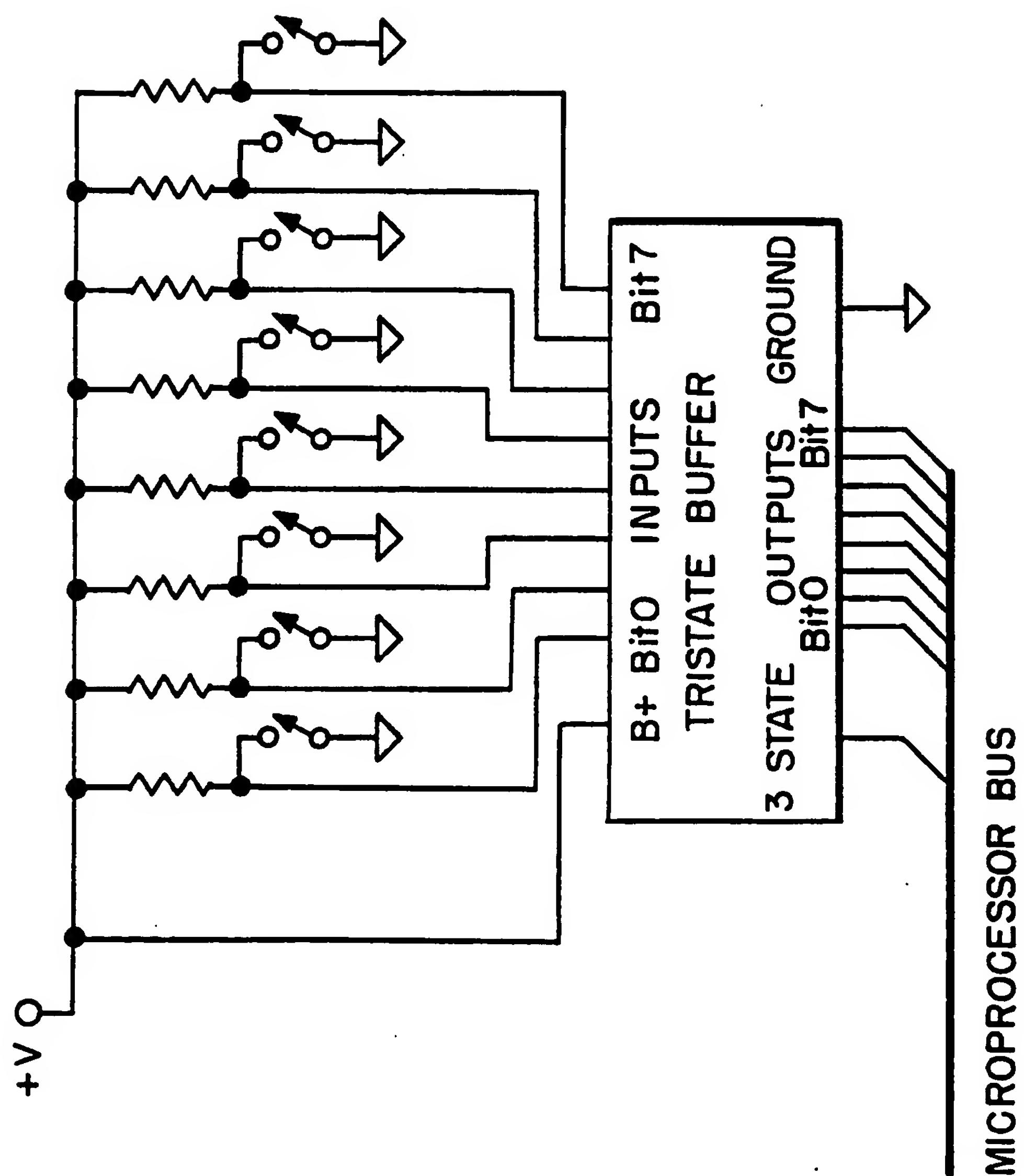
FIGURE 6A

OVERVIEW of PROTOCOL for CLOSING
the THERAPEUTIC LOOP

12 / 12

DONE ONLY AT VISITS TO PHYSICIAN

COMPARISON TO TARGET VALUES

AUDITORY AND/OR VISUAL FEEDBACK TO PATIENT

TIMING OF BREATH HOLDING WITH SIGNAL TO PATIENT AT END

READING OF DATA BACK INTO CLINICAL WORKSTATION

ANALYSIS INCLUDING COMPARISON TO PREVIOUS STORED PERIODS IN CLINICAL WORKSTATION

REMINDER TO PATIENT OF TIME TO TAKE MEDICATION

PATIENT INDICATES READY AND SHAKES THE DEVICE TO PREPARE THE MEDICATION

TRIGGER DISCHARGE

RECORD DATA INCLUDING RELEASE OF AEROSOL, AIR-FLOW TIME COURSE, TIME AND DATA STAMP

CALCULATION OF DERIVED VALUES

FIGURE 6B

PROCESS for UTILIZATION by the PATIENT